REMARKS

Claims 1-9, 43-62, and 84-88 are pending in the application. Claims 10-42, 63-83, and 89-92 have been canceled, and claims 1-9, 43-62, and 84-88 have been amended. The specification has been amended to add the priority claim and insert the Sequence Listing and sequence identifiers in the specification. Support for the amendments can be found in the specification at, e.g., page 14, lines 7-20, and page 15, line 13, to page 17, line 22. These amendments add no new matter.

Page 16 of Paper Number 14

On page 2 of the Office Action, the Examiner stated that page 16 of paper number 14 is missing from the file. A copy of the missing page is enclosed with the present response.

Sequence Disclosure Rule Compliance

Applicants submit herewith a Sequence Listing in computer-readable form as required by 37 CFR § 1.824. In addition, applicants submit a paper copy of the Sequence Listing as required under 37 CFR § 1.823(a) and a statement under 37 CFR §1.821(f). Applicants hereby submit that the enclosures fulfill the requirements under 37 C.F.R. §1.821-1825.

Drawings

On page 4 of the Office Action, the Examiner stated that the formal drawings submitted by applicants with paper number 14 are not in the file. The Examiner requested that applicants submit corrected drawings with the present response. Applicants enclose copies of the formal drawings and the transmittal page as enclosed with the submission originally submitted to the Patent & Trademark Office on April 30, 2002.

Priority

On pages 4-5 of the Office Action, the Examiner stated that reference to all prior applications to which applicants claim priority must be inserted on the first page of the

application. The specification has been amended by the current amendment to add the priority claim to the first page of the application.

35 U.S.C. § 101

On page 5 of the Office Action, the Examiner rejected claims 1-9, 43-62, and 84-88 as allegedly directed to non-statutory subject matter. According to the Examiner, the claims

> are drawn to a ligand profile comprising simply a list of different polypeptide ligands. Such a ligand profile is merely a compilation or arrangement of data or facts, and is considered as nonfunctional descriptive material. "When nonfunctional descriptive material is recorded on some computer-readable medium, it is not statutory since no requisite functionality is present to satisfy the practical application requirement. Merely claiming nonfunctional descriptive material stored in a computer-readable medium does not make it statutory" (MPEP § 2106 IV (B)(1).

Applicants respectfully traverse the rejection in light of the amendments to the claims and the following comments. As amended, independent claims 1-5 are directed to a set of polypeptide ligands produced in a cell. The claimed set of polypeptide ligands constitutes a composition of matter, which is statutory subject matter for under section 101. The amendments to the claims obviate the Examiner's contention that a "ligand profile" is non-statutory subject matter. In light of these amendments, applicants request that the Examiner withdraw the rejection of independent claims 1-5 and the claims that depend therefrom.

On pages 5-6 of the Office Action, the Examiner rejected claims 1-9, 43-62, and 84-88 as allegedly lacking patentable utility. In a related rejection on page 6, the Examiner rejected the claims as allegedly not enabled. According to the Examiner, the claims

> are drawn to a ligand profile which is merely a compilation or arrangement of data or facts. The specification states that such a profile can be used to compare with other profiles in identifying cellular targets useful in diagnostics, drug screening and development, etc. See page 5, lines 25-33, pages 82-84. This utility is not deemed specific because no identification of specific disease, specific target and/or specific drug is asserted. Further, the claimed profile is not supported by a substantial utility because no substantial utility has been established for the claimed subject matter. For example, in the aforementioned utility, it takes further research to determine what disease, specific target and/or specific drug can be identified. The apparent need for such research clearly

indicates that the profile is not disclosed as to a currently available or substantial utility. Similarly, the other listed and asserted utilities in the instant specification are neither substantial nor specific.

Furthermore, neither the specification as filed nor any art of record discloses or suggests any non-asserted well-established utility for the claimed ligand profile.

Applicants respectfully traverse the rejection in light of the amendments to the claims and the following comments. As amended, independent claims 1-5 are directed to a set of polypeptide ligands produced by a cell. The claimed set of polypeptide ligands is supported by a specific, substantial, and credible utility.

The claimed set of polypeptide ligands constitutes a reproducible characteristic of a cell. As such, the set can be used in a variety of methods intended to exploit the characterization of the protein content of a given cell. The set of ligands can be used to catalogue the proteins expressed and turned over in a cell for any particular cell type or metabolic state. For example, a characteristic fingerprint of polypeptide ligands can be generated for a given cell type, for diseased vs. normal cells, or for different metabolic or developmental states of a cell. Comparison of the claimed set of polypeptide ligands with the set of ligands detected in a different cell type or metabolic state can assist in the identification of targets useful in diagnostics, drug screening and development, and for developing therapeutic regimens. The claimed set of ligands can thus be used, for example, to indicate particular polypeptides that are either present or absent in a diseased state. Such a use of the claimed sets is generally applicable for carrying out screens of a wide variety of cells or cell types, and is not limited to particular diseases. Accordingly, and contrary to the comments of the Examiner on page 6 of the Office Action, no specific disease or drug target need be asserted to establish the specific and substantial utility of the claimed set for cataloguing the protein content of a cell and using such a set to identify proteins predicted to be associated with a disease state.

In light of these comments, applicants request that the Examiner withdraw the rejections.

35 U.S.C. § 103(a)

On pages 7-8 of the Office Action, the Examiner rejected claims 1-5, 8, 9, 45, 46, 49-51, 54-56, 59-62, and 84-88 as allegedly unpatentable over Hynes et al. (1996) FASEB J. 10:137-147 ("Hynes"). According to the Examiner

> Hynes et al. disclose a method of isolating the binding partners of a chaperone protein, chaperonin-containing TCP-1 and establish a binding profile for the protein with its partners in testis cells. See Abstract. The TCP-1 protein is interpreted as a receptor and the binding partners as ligands. The profile includes 32 proteins/polypeptides and each is characterized based upon at least 3 different physical or chemical attributes: pI, molecular weight, database accession number for sequence listing, and spot number on the two-D gel with which the proteins are isolated. See Table I. Further, Hynes et al. also disclose the peptide mass fingerprints for spot 27. See Fig. 2.
>
> While Hynes et al. do not explicitly disclose that this binding profile is characteristics for a given cell, they do disclose that TCP-1 and its partners are isolated from mouse testis cells. It would have been obvious to an ordinary sill in the art that the profile is characteristics of mouse testis cells.

Applicants respectfully traverse the rejection. As amended, the claims are directed to sets of polypeptide ligands that are produced in a cell and bind to a single type of multi-ligand binding receptor in the cell. Hynes does not disclose or suggest the claimed sets of polypeptide ligands.

Hynes describes the partial characterization of a subset of proteins present in mouse testis, via 20S sucrose gradient fractionation of all testis proteins followed by two dimensional gel electrophoresis. As detailed by Hynes, the chaperonin-containing protein TCP-1 ("CCT") sediments at 20S in a sucrose gradient and accounts for about 70% of the total mouse testis protein in the 20S fraction. Hynes nowhere indicates that the remaining 30% of the protein content of the 20S sucrose gradient fraction constitutes only proteins that bind to CCT. Instead, Hynes properly characterizes the non-CCT proteins in the 20S fraction as proteins that "copurify" with CCT. For example, Hynes explains that components of certain high molecular weight complexes are believed to be of a size that causes them to co-sediment with CCT in the 20S sucrose gradient fraction (Hynes at page 145). Such co-purification of these high molecular weight complexes would therefore not be expected to be the result of an interaction between CCT and the co-purified protein. Because the claimed set of polypeptide ligands requires that

each of the polypeptide ligands contained in the set bind to a particular multi-ligand binding receptor present in a cell, the collection of proteins identified by Hynes as present in the 20S sucrose gradient fraction does not constitute the claimed "set of polypeptide ligands."

The "reference profile" described by Hynes is merely a partial characterization of several proteins contained in a 20S sucrose gradient fraction of proteins present in mouse testis. The "reference profile" of Hynes is not a listing of proteins identified as constituting polypeptide ligands of CCT. Furthermore, Hynes contains no suggestion or motivation to modify its experimental protocol to identify only those proteins in a particular cell type that bind to CCT. In addition, Hynes gives no reason for the person of ordinary skill in the biological arts to expect that, were one to attempt identify those proteins in a cell that bind to CCT, that such proteins would constitute 10 or more distinct polypeptide ligands as is required of the claimed invention.

In light of the amendments to the claims and the comments provided herein, applicants respectfully request that the Examiner withdraw the rejection.

On page 8 of the Office Action, the Examiner rejected claims 1-9, 43-62, and 84-88 as allegedly unpatentable over Hynes in view of Brusic et al. (1998) Nucleic Acids Res. 26:368 ("Brusic"). According to the Examiner

> [f]or claims 6-7, 43-44, 47-48, 52-53 and 57-58, Hynes et al. do not disclose a profile for MHC class I or II receptor. However, Hynes et al. state that the method they use to establish the profile for TCP-1, i.e. the mass spectrometry and database matching, is advantageous over traditional methods and is less laborious and fast, thus motivating using the method for establishing profiles for other proteins. See page 137, right column. Brusic et al. establish a profile for MHC class I or II including over 13000 peptide sequences. Brusic et al. state that such a profile would facilitate research on antigen processing, etc. However, the profile compiles peptides from different cell sources of different publications and Brusic et al. admit that potential errors exist. See page 370, left column. An ordinary sill in the art would have been motivated by Hynes et al. to use their strategy to establish a profile for MHC class I or II to obtain peptides from a single cell or single cell type so as to prevent the potential errors existed in Brusic et al.'s profile. Therefore, a profile of MHC class I or II would have been obvious to an ordinary sill in the art at the time the instant invention was made.

Applicants respectfully traverse the rejection. As detailed above, Hynes does not describe or suggest the claimed set of polypeptide ligands that bind to a single type of multi-

ligand binding receptor in a cell. In addition, and contrary to the Examiner's comment on page 8 of the Office Action stating that Hynes established a "profile for TCP-1," Hynes did not characterize a discrete group of proteins that constitute polypeptide ligands for CCT. Instead, Hynes disclosed the partial characterization of several proteins from mouse testis that are contained in a 20S sucrose gradient fraction, irrespective of whether such proteins bind to CCT.

Brusic does not add what Hynes is lacking. The MHCPEP database of Brusic is not a set of polypeptide ligands that is a reproducible characteristic for a given cell. Brusic's database contains a description of over 13,000 peptide sequences that have been found to bind to a wide variety of MHC class I or class II molecules. Brusic's database was compiled by analyzing published reports describing MHC class I or class II-binding peptides as well as by obtaining direct submissions of experimental data on such peptides. Brusic's database constitutes a profile of MHC binding peptides, but provides no characterization whatsoever of a cell that may contain either the peptides or their corresponding proteins. Brusic provides no suggestion or motivation to modify the experimental protocol of Hynes to characterize the set of polypeptide ligands in a particular cell or cell type that bind to an MHC class I or II molecule or any other multi-ligand binding receptor. Brusic's extensive database of MHC-binding peptides does not suggest to ordinary biologist to prepare a ser of MHC class I or class II-binding peptides to characterize the protein content of a cell.

Neither Hynes nor Brusic, taken alone or in combination, suggest creating a set of at least ten different polypeptide ligands that are produced in a cell and bind to a single type of multi-ligand binding receptor in the same cell. In light of these deficiencies, applicants submit that the cited references do not render the claimed invention obvious. Accordingly, applicants request that the Examiner withdraw the rejection.